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| 10/066,293 | 01/31/2002 | Maria-Grazia Ascenzi | 4079/1I235US2 | 2056 |

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| EXAMINER | |
|---|---|
| THANGAVELU, KANDASAMY | |
| **ART UNIT** | **PAPER NUMBER** |
| 2123 | |

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/066,293 | ASCENZI ET AL. | |
| | **Examiner** | **Art Unit** | |
| | Kandasamy Thangavelu | 2123 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 November 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *15 November 2004*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

## DETAILED ACTION

1. This communication is in response to the Applicants' Amendment dated November 15, 2004. Claims 1, 2, 10, 17 and 20 were amended. Claims 1-26 of the application are pending. This office action is made non-final.

### *Information Disclosure Statement*

2. Acknowledgment is made of the information disclosure statements filed on November 15, 2004, together with copies of the papers. The papers and patents have been considered in reviewing the claims.

### *Drawings*

3. The drawings submitted on November 15, 2004 are objected to. The bottom margins in Figures 1C, 7A, 11, 13 and 16 are inadequate. A minimum of 1 cm margin is required at the bottom of all drawings. Applicants are required to send corrected drawings in response to this office action.

### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 23- 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

5.1 Claim 23 states, "The method of claim 22, wherein angle-of-twist as a function of torque is determined by quasi-static torsional loading to rupture". Therefore it is clear that this process is a laboratory process using the torsional loading of the osteon of the bone until rupture. However, the method of preparing the model of the viscoelastic properties of the bone is a software process which involves correlating different parameters of the model. The software process of model building is done on a computer in non-real time. The specification does not describe how the quasi-static torsional loading of the osteon of the bone that is done in the laboratory is interfaced with the method of preparing the model of the viscoelastic properties of the bone that is done on a computer in non-real time. Is the laboratory testing controlled by the model building process? What is the interface mechanism between the laboratory testing that is done as part of model building and the model building process that is done on a computer using a stochastic modeling software in non-real time?

5.2 Claim 24 states, "The method of claim 21, comprising determining the ratio of collagen and mucopolysaccharides in a longitudinal osteon as compared to those of an alternate osteon by the following method:

(i) drying the longitudinal and alternate osteons to constant weight;

(ii) separately contacting the longitudinal and alternate osteons with acid to promote the hydrolysis of collagen to hydroxyproline and mucopolysaccharides to hexosamine; and

(iii) separating hydroxyproline from hexosamine; and

(iv) determining the ratio of hydroxyproline and hexosamine in the longitudinal osteon as compared to the alternate osteon;

wherein the ratio of hydroxyproline and hexosamine in the longitudinal osteon as compared to the alternate osteon corresponds to the ratio of collagen and mucopolysaccharides in the longitudinal osteon as compared to the alternate osteon". Therefore it is clear that this process is a laboratory process using various physical elements and physical processes. However, the method of preparing the model of the viscoelastic properties of the bone is a software process which involves correlating different parameters of the model. The software process of model building is done on a computer in non-real time. The specification does not describe how the method of determining the ratio of collagen and mucopolysaccharides in a longitudinal osteon as compared to those of an alternate osteon by that is done in the laboratory using physical elements and physical processes is interfaced with the method of preparing the model of the viscoelastic properties of the bone that is done on a computer in non-real time. Is the laboratory testing controlled by the model building process? What is the interface mechanism between the laboratory testing that is done as part of model building and the model

building process that is done on a computer using a stochastic modeling software in non-real time?

5.3 Claim 26 states, "The method of claim 21, wherein the collagen-bundle direction related to osteon axis is determined by circularly polarizing light microscopy, confocal microscopy or X-ray diffraction". Therefore it is clear that this process of determining the collagen-bundle direction related to osteon axis is a laboratory process using circularly polarizing light microscopy, confocal microscopy or X-ray diffraction. However, the method of preparing the model of the viscoelastic properties of the bone is a software process which involves correlating different parameters of the model. The software process of model building is done on a computer in non-real time. The specification does not describe how this process of determining the collagen-bundle direction related to osteon axis using circularly polarizing light microscopy, confocal microscopy or X-ray diffraction that is done in the laboratory is interfaced with the method of preparing the model of the viscoelastic properties of the bone that is done on a computer in non-real time. Is the laboratory testing controlled by the model building process? What is the interface mechanism between the laboratory testing that is done as part of model building and the model building process that is done on a computer using a stochastic modeling software in non-real time?

Claims rejected but not specifically addressed are rejected based on their dependency on rejected claims.

### *Claim Rejections - 35 USC § 101*

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1-26 are rejected under 35 U.S.C. 101 because the claimed inventions are directed to non-statutory subject matter.

7.1 Independent claim 1 recites a model of compact adult bone, wherein said model comprises the viscoelastic properties of at least one type of an osteon. The limitations recited in claim state that each viscoelastic property is correlated with at least one component of bone microstructure and ultrastructure, and components are grouped hierarchically to provide a description of one or more characteristics of the bone which are all mathematical models or software components. Therefore it appears that the model of compact adult bone is a set of mathematical equations or software which is not statutory subject matter. To be statutory, the claim should refer to a system or apparatus comprising hardware elements and software components, wherein the software components would comprise a model of compact adult bone.

The limitations recited in dependent claims 2-16 contain descriptions of the characteristics of the bone or viscoelastic properties which are not statutory subject matter.

7.2 Method claims 17-18 are rejected for reciting a process that is not directed to the technological arts.

Regarding claim 17, this claim is directed at a method of predicting deformation and fractures of compact adult bone comprising using a model of compact adult bone, wherein the model comprises the viscoelastic properties of longitudinal and alternate osteons, whereas none of the limitations describe any type of computer-implemented steps. To be statutory, the utility of an invention must be within the technological arts. *In re Musgrave*, 167 USPQ 280, 289-90 (CCPA, 1970). The definition of "technology" is the "application of science and engineering to the development of machines and procedures in order to enhance or improve human conditions, or at least to improve human efficiency in some respect." (Computer Dictionary 384 (Microsoft Press, 2d ed. 1994)).

Dependent claim 18 depends on Claim 17 but does not add further statutory steps. The limitations recited in claim 18 contain no language suggesting this claim is intended to be within the technological arts.

7.3 Regarding claim 19, this claim is directed at a method of identifying the requirements of bone reconstruction and prosthesis using the model, whereas none of the limitations describe any type of computer-implemented steps. To be statutory, the utility of an invention must be within the technological arts.

7.4 Method claims 20-26 are rejected for reciting a process that is not directed to the technological arts.

Regarding claim 20, this claim is directed at a method of preparing a model of the viscoelastic properties of bone, whereas none of the limitations describe any type of computer-

implemented steps. To be statutory, the utility of an invention must be within the technological arts.

Dependent claims 21-26 depend on Claim 20 but do not add further statutory steps. The limitations recited in claims 21-26 contain no language suggesting these claims are intended to be within the technological arts.

8.1 Claims 1- 16 would be statutory if claim 1 is rewritten as a system or apparatus claim comprising hardware elements and software components, wherein the software components comprise model of compact adult bone comprising ...

8.2 Claims 17 and 18 would be statutory if claim 17 is rewritten as a computer implemented method of predicting deformation and fractures of compact adult bone comprising using a model of compact adult bone...

8.3 Claim 19 would be statutory if claim 19 is rewritten as a computer implemented method of identifying the requirements of bone reconstruction and prosthesis using the model...

8.4 Claims 20-26 would be statutory if claim 20 is rewritten as a computer implemented method of preparing a model of the viscoelastic properties of bone...

## *Claim Rejections - 35 USC § 102*

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claim 20 is rejected under 35 U.S.C. § 102(b) as being anticipated by **Crolet et al.** ("Compact Bone: Numerical simulation of mechanical characteristics", J. Biomechanics, Vol. 26, No. 6, 1993).

10.1 **Crolet et al.** teaches methods, apparatus and computer program products for automated visual inspection. Specifically, as per claim 20, **Crolet et al.** teaches a method of preparing a model of the viscoelastic properties of bone, wherein the method comprises determining viscoelastic properties of alternate and longitudinal osteons (Page 677, Abstract; Page 677, CL2, Para 1 to Para 2; Page 678, CL2, Para 4 to Page 682, CL2, Para 3; Page 683, CL1, Para 3 and 4).

### *Claim Rejections - 35 USC § 103*

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

12. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 1, 2 and 10 are rejected under 35 U.S.C. § 102(b) as being unpatentable over **Crolet et al.** ("Compact Bone: Numerical simulation of mechanical characteristics", J. Biomechanics, Vol. 26, No. 6, 1993) in view of **Ascenzi** ("A first estimation of prestress in so-called circularly fibred osteonic lamellae", March 1999), and further in view of **Lakes** ("Materials with structural hierarchy", Nature 361, February 1993).

13.1 As per claim 1, **Crolet et al.** teaches a model of compact adult bone, wherein the model comprises the viscoelastic properties of at least one type of a secondary osteon (Page 677, Abstract; Page 677, CL2, Para 1 to Para 2; Page 678, CL2, Para 4 to Page 682, CL2, Para 3).

**Crolet et al.** does not expressly teach that each viscoelastic property is correlated with at least one component of bone microstructure and ultrastructure, and components are grouped hierarchically to provide a description of one or more characteristics of the bone. **Ascenzi** (March 1999) teaches that the each viscoelastic property is correlated with at least one component of bone microstructure and ultrastructure, and components are grouped hierarchically to provide a description of one or more characteristics of the bone (Abstract, L1-3, L5-8 and L9-

13; Page 935, CL1, Para 1, L3-5), because the use of hierarchical structure involving the microstructure of the osteonic lamellae and the ultra structure of the collagen bundles allows formulation of hypotheses on lamellar stiffness and other mechanical properties and yields hypotheses on bone ultra- and micro structures (Abstract, L9-13; Page 935, CL1, Para 1, L3-5). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the model of **Crolet et al.** with the model of **Ascenzi** (March 1999) that included each viscoelastic property being correlated with at least one component of bone microstructure and ultrastructure, and components being grouped hierarchically to provide a description of one or more characteristics of the bone. The artisan would have been motivated because the use of hierarchical structure involving the microstructure of the osteonic lamellae and the ultra structure of the collagen bundles would allow formulation of hypotheses on lamellar stiffness and other mechanical properties and would yield hypotheses on bone ultra- and micro structures.

In addition, **Lakes** also teaches that the each viscoelastic property is correlated with at least one component of bone microstructure and ultrastructure, and components are grouped hierarchically to provide a description of one or more characteristics of the bone (Page 5, Fig. 4; Page 5, Para 1, L1-8; Page 1, Para 2, L1-16; Page 2, Para 3, L1-6; Page 5, Par 1, L12-17), because the structural hierarchy can play a major role in determining the bulk material properties; understanding the effects of the hierarchical structure can guide the synthesis of new materials with physical properties tailored for specific applications (Page 1, Para 1); the idea of hierarchical structure can be the basis for synthesis of new microstructures which give rise to enhanced and useful physical properties such as improved strength and toughness (Page 1, Para 2, L16-19). It would have been obvious to one of ordinary skill in the art at the time of

Applicants' invention to modify the model of **Crolet et al.** with the model of **Lakes** that included each viscoelastic property being correlated with at least one component of bone microstructure and ultrastructure, and components being grouped hierarchically to provide a description of one or more characteristics of the bone. The artisan would have been motivated because the structural hierarchy could play a major role in determining the bulk material properties; understanding the effects of the hierarchical structure could guide the synthesis of new materials with physical properties tailored for specific applications; the idea of hierarchical structure could be the basis for synthesis of new microstructures which would give rise to enhanced and useful physical properties such as improved strength and toughness.

Per claim 2: **Crolet et al.** teaches that the secondary osteon is a longitudinal osteon or an alternate osteon (Page 683, CL1, Para 3 and 4).

Per claim 10: **Crolet et al.** teaches the model comprising the viscoelastic properties of longitudinal and alternate osteons (Page 683, CL1, Para 3 and 4).

14. Claims 3, 4 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Crolet et al.** ("Compact Bone: Numerical simulation of mechanical characteristics", J. Biomechanics, Vol. 26, No. 6, 1993) in view of **Ascenzi** ("A first estimation of prestress in so-called circularly fibred osteonic lamellae", March 1999), and **Lakes,** ("Materials with structural hierarchy", Nature 361, February 1993), and further in view of **Carter et al.** ("Mechanical properties and composition of Cortical Bone", March 1978) and **Wolfinbarger, Jr. et al.** (U.S. Patent 6,293,970).

14.1 As per claim 3, **Crolet et al., Ascenzi** (March 1999) and **Lakes** teach the model of claim 1. **Crolet et al.** teaches that viscoelastic properties comprises at least one parameter selected from the group consisting of collagen content (Page 679, CL2, Para 1; Page 684 CL2, Para 2), hydroxyapatite content (Page 679, CL1, Para 3; Page 679, CL2, Para 1; Page 684 CL2, Para 4), collagen bundle orientation relative to osteon axis (Page 683, CL1, Para 3 and 4) and content of porosity fluids (Page 677, CL2, Para 2).

**Crolet et al.** does not expressly teach that the viscoelastic properties comprises at least one parameter selected from the group consisting of mechanical properties. **Carter et al.** teaches that the viscoelastic properties comprises at least one parameter selected from the group consisting of mechanical properties (Page 192, CL2, Para 2; Page 192, CL1, Para 1), because the changes in mechanical properties affect the response of the bone to imposed loads, making the bone more or less resistant to fracture (Page 192, CL2, Para 2). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the model of **Crolet et al.** with the model of **Carter et al.** that included the viscoelastic properties comprising at least one parameter selected from the group consisting of mechanical properties. The artisan would have been motivated because the changes in mechanical properties would affect the response of the bone to imposed loads, making the bone more or less resistant to fracture.

**Crolet et al.** does not expressly teach that the viscoelastic properties comprises at least one parameter selected from the group consisting of mucopolysaccharide content. **Wolfinbarger, Jr. et al.** teaches that the viscoelastic properties comprises at least one

parameter selected from the group consisting of mucopolysaccharide content (CL1, L30-32), because the bone tissue comprises osteoid and minerals; and the osteoid contains non-sulfated mucopolysaccharides (CL1, L28-32) and as per **Carter et al.** the relationships between stresses and strains at a particular point in the bone are governed by the material properties of the local bone tissues (Page 192, CL1, Para 1). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the model of **Crolet et al.** with the model of **Wolfinbarger, Jr. et al.** that included the viscoelastic properties comprising at least one parameter selected from the group consisting of mucopolysaccharide content. The artisan would have been motivated because the bone tissue comprises osteoid and minerals; and the osteoid contains non-sulfated mucopolysaccharides and the relationships between stresses and strains at a particular point in the bone are governed by the material properties of the local bone tissues.

**Crolet et al.** does not expressly teach that the viscoelastic properties comprises at least one parameter selected from the group consisting of osteocyte content. **Wolfinbarger, Jr. et al.** teaches that the viscoelastic properties comprises at least one parameter selected from the group consisting of osteocyte content (CL1, L36-40), because the bone tissue is laid down around the osteocytes and these cells are found in small interconnected channels which are interconnected through the Haversian canal system (CL1, L36-40) and the bone tissue is organized into osteons made up of collagen fiber bundles whose orientation affect the mechanical behavior of the osteons (CL1, L40-49). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the model of **Crolet et al.** with the model of **Wolfinbarger, Jr. et al.** that included the viscoelastic properties comprising at least one parameter selected from the group consisting of osteocyte content. The artisan would have been motivated because the

bone tissue is laid down around the osteocytes and these cells are found in small interconnected channels which are interconnected through the Haversian canal system and the bone tissue is organized into osteons made up of collagen fiber bundles whose orientation affect the mechanical behavior of the osteons.

**Crolet et al.** does not expressly teach that the viscoelastic properties comprises at least one parameter selected from the group consisting of osteoblast content. **Carter et al.** teaches that the viscoelastic properties comprises at least one parameter selected from the group consisting of osteoblast content (Page 194, CL2, Para 2), because osteoblasts surround the bone surface in woven fibred bone; these osteoblasts deposit successive layers of new bone forming the lamellae of secondary Osteons; these microstructural characteristics affect the mechanical properties of the bone tissue (Page 194, CL2, Para 2 to Page 195, CL1, Para 1; Page 192, CL2, Para 2). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the model of **Crolet et al.** with the model of **Carter et al.** that included the viscoelastic properties comprising at least one parameter selected from the group consisting of osteoblast content. The artisan would have been motivated because osteoblasts surround the bone surface in woven fibred bone; these osteoblasts deposit successive layers of new bone forming the lamellae of secondary Osteons; these microstructural characteristics would affect the mechanical properties of the bone tissue.

14.2 As per claim 4, **Crolet et al., Ascenzi** (March 1999), **Lakes, Carter et al.** and **Wolfinbarger, Jr. et al.** teach the model of claim 3. **Crolet et al.** teaches that viscoelastic properties comprises collagen content (Page 679, CL2, Para 1; Page 684 CL2, Para 2),

hydroxyapatite content (Page 679, CL1, Para 3; Page 679, CL2, Para 1; Page 684 CL2, Para 4) and collagen bundle orientation relative to osteon axis (Page 683, CL1, Para 3 and 4).

**Crolet et al.** does not expressly teach that the viscoelastic properties comprises mechanical properties. **Carter et al.** teaches that the viscoelastic properties comprises mechanical properties (Page 192, CL2, Para 2; Page 192, CL1, Para 1), because the changes in mechanical properties affect the response of the bone to imposed loads, making the bone more or less resistant to fracture (Page 192, CL2, Para 2). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the model of **Crolet et al.** with the model of **Carter et al.** that included the viscoelastic properties comprising mechanical properties. The artisan would have been motivated because the changes in mechanical properties would affect the response of the bone to imposed loads, making the bone more or less resistant to fracture.

**Crolet et al.** does not expressly teach that the viscoelastic properties comprises mucopolysaccharide content. **Wolfinbarger, Jr. et al.** teaches that the viscoelastic properties comprises mucopolysaccharide content (CL1, L30-32), because the bone tissue comprises osteoid and minerals; and the osteoid contains non-sulfated mucopolysaccharides (CL1, L28-32) and as per **Carter et al.** the relationships between stresses and strains at a particular point in the bone are governed by the material properties of the local bone tissues (Page 192, CL1, Para 1). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the model of **Crolet et al.** with the model of **Wolfinbarger, Jr. et al.** that included the viscoelastic properties comprising mucopolysaccharide content. The artisan would have been

motivated because the bone tissue comprises osteoid and minerals; and the osteoid contains non-sulfated mucopolysaccharides and the relationships between stresses and strains at a particular point in the bone are governed by the material properties of the local bone tissues.

14.3 As per claim 11, **Crolet et al., Ascenzi** (March 1999) and **Lakes** teach the model of claim 10. **Crolet et al.** teaches that viscoelastic properties comprises collagen content (Page 679, CL2, Para 1; Page 684 CL2, Para 2), hydroxyapatite content (Page 679, CL1, Para 3; Page 679, CL2, Para 1; Page 684 CL2, Para 4) and collagen bundle orientation relative to osteon axis (Page 683, CL1, Para 3 and 4).

**Crolet et al.** does not expressly teach that the viscoelastic properties comprises mechanical properties. **Carter et al.** teaches that the viscoelastic properties comprises mechanical properties (Page 192, CL2, Para 2; Page 192, CL1, Para 1), because the changes in mechanical properties affect the response of the bone to imposed loads, making the bone more or less resistant to fracture (Page 192, CL2, Para 2). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the model of **Crolet et al.** with the model of **Carter et al.** that included the viscoelastic properties comprising mechanical properties. The artisan would have been motivated because the changes in mechanical properties would affect the response of the bone to imposed loads, making the bone more or less resistant to fracture.

**Crolet et al.** does not expressly teach that the viscoelastic properties comprises mucopolysaccharide content. **Wolfinbarger, Jr. et al.** teaches that the viscoelastic properties

comprises mucopolysaccharide content (CL1, L30-32), because the bone tissue comprises osteoid and minerals; and the osteoid contains non-sulfated mucopolysaccharides (CL1, L28-32) and as per **Carter et al.** the relationships between stresses and strains at a particular point in the bone are governed by the material properties of the local bone tissues (Page 192, CL1, Para 1). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the model of **Crolet et al.** with the model of **Wolfinbarger, Jr. et al.** that included the viscoelastic properties comprising mucopolysaccharide content. The artisan would have been motivated because the bone tissue comprises osteoid and minerals; and the osteoid contains non-sulfated mucopolysaccharides and the relationships between stresses and strains at a particular point in the bone are governed by the material properties of the local bone tissues.

15. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Crolet et al.** ("Compact Bone: Numerical simulation of mechanical characteristics", J. Biomechanics, Vol. 26, No. 6, 1993) in view of **Carter et al.** ("Mechanical properties and composition of Cortical Bone", March 1978), and further in view of **Wolfinbarger, Jr. et al.** (U.S. Patent 6,293,970).

15.1 As per Claim 21, **Crolet et al.** teaches the method of claim 20. **Crolet et al.** teaches that viscoelastic properties comprises collagen content (Page 679, CL2, Para 1; Page 684 CL2, Para 2), hydroxyapatite content (Page 679, CL1, Para 3; Page 679, CL2, Para 1; Page 684 CL2, Para 4) and collagen bundle orientation relative to osteon axis (Page 683, CL1, Para 3 and 4).

**Crolet et al.** does not expressly teach that the viscoelastic properties comprises mechanical properties. **Carter et al.** teaches that the viscoelastic properties comprises mechanical properties (Page 192, CL2, Para 2; Page 192, CL1, Para 1), because the changes in mechanical properties affect the response of the bone to imposed loads, making the bone more or less resistant to fracture (Page 192, CL2, Para 2). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the method of **Crolet et al.** with the method of **Carter et al.** that included the viscoelastic properties comprising mechanical properties. The artisan would have been motivated because the changes in mechanical properties would affect the response of the bone to imposed loads, making the bone more or less resistant to fracture.

**Crolet et al.** does not expressly teach that the viscoelastic properties comprises mucopolysaccharide content. **Wolfinbarger, Jr. et al.** teaches that the viscoelastic properties comprises mucopolysaccharide content (CL1, L30-32), because the bone tissue comprises osteoid and minerals; and the osteoid contains non-sulfated mucopolysaccharides (CL1, L28-32) and as per **Carter et al.** the relationships between stresses and strains at a particular point in the bone are governed by the material properties of the local bone tissues (Page 192, CL1, Para 1). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the method of **Crolet et al.** with the method of **Wolfinbarger, Jr. et al.** that included the viscoelastic properties comprising mucopolysaccharide content. The artisan would have been motivated because the bone tissue comprises osteoid and minerals; and the osteoid contains non-sulfated mucopolysaccharides and the relationships between stresses and strains at a particular point in the bone are governed by the material properties of the local bone tissues.

16. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Crolet et al.** ("Compact Bone: Numerical simulation of mechanical characteristics", J. Biomechanics, Vol. 26, No. 6, 1993) in view of **Ascenzi** ("A first estimation of prestress in so-called circularly fibred osteonic lamellae", March 1999), and **Lakes,** ("Materials with structural hierarchy", Nature 361, February 1993), and further in view of **Carter et al.** ("Mechanical properties and composition of Cortical Bone", March 1978), **Wolfinbarger, Jr. et al.** (U.S. Patent 6,293,970)and **Ascenzi et al.** ("The torsional properties of single selected osteons", October 1993).

16.1 As per claim 5, **Crolet et al., Ascenzi** (March 1999)**, Lakes, Carter et al.** and **Wolfinbarger, Jr. et al.** teach the model of claim 3. **Crolet et al.** teaches that osteon mechanical properties comprises hydroxyapatite content (Page 679, CL1, Para 3; Page 679, CL2, Para 1; Page 684 CL2, Para 4).

**Crolet et al.** does not expressly teach that osteon mechanical properties comprises an angle-of-twist as a function of torque. **Ascenzi et al.** (October 1993) teaches that osteon mechanical properties comprises an angle-of-twist as a function of torque (Abstract; Page 875, CL2, Para 3; Page 880, Fig. 4), as the longitudinal osteons indicate most resistance to torsional loading; and the transverse osteons have low resistance to torsional loading (Abstract, L8-10). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the model of **Crolet et al.** with the model of **Ascenzi et al.** (October 1993) that included osteon mechanical properties comprising an angle-of-twist as a function of torque. The artisan

would have been motivated because the longitudinal osteons would indicate most resistance to torsional loading; and the transverse osteons would have low resistance to torsional loading.

**Crolet et al.** does not expressly teach that osteon mechanical properties comprises an angle-of-twist as a function of strain rate or time. **Ascenzi et al.** (October 1993) teaches that osteon mechanical properties comprises an angle-of-twist as a function of strain rate or time (Page 879, CL1, Para 5 to Page 879, CL2, Para 1), as the osteon failure depends on the strain rate and time (Page 879, CL1, Para 5 to Page 879, CL2, Para 1). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the model of **Crolet et al.** with the model of **Ascenzi et al.** (October 1993) that included osteon mechanical properties comprising an angle-of-twist as a function of strain rate or time. The artisan would have been motivated because the osteon failure would depend on the strain rate and time.

16.2 As per claim 6, **Crolet et al., Ascenzi** (March 1999)**, Lakes, Carter et al., Wolfinbarger, Jr. et al.** and **Ascenzi et al.** (October 1993) teach the model of claim 5.

**Crolet et al.** does not expressly teach that the angle-of-twist as a function of torque is derived from tests conducted under monotonic or dynamic loading. **Ascenzi et al.** (October 1993) teaches that the angle-of-twist as a function of torque is derived from tests conducted under monotonic or dynamic loading (Page 879, CL1, Para 5 to Page 879, CL2, Para 1; Page 880, CL1, Para 4 to Page 881, CL2, Para 1; Page 880, Fig. 4), as the stress and strain produced during application of the progressive loading allows determination of the unchecked twisting of the specimen indicating osteon failure (Page 879, CL1, Para 5 to Page 879, CL2, Para 1). It

would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the model of **Crolet et al.** with the model of **Ascenzi et al.** (October 1993) that included the angle-of-twist as a function of torque being derived from tests conducted under monotonic or dynamic loading. The artisan would have been motivated because the stress and strain produced during application of the progressive loading would allow determination of the unchecked twisting of the specimen indicating osteon failure.

17. Claims 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Crolet et al.** ("Compact Bone: Numerical simulation of mechanical characteristics", J. Biomechanics, Vol. 26, No. 6, 1993) in view of **Carter et al.** ("Mechanical properties and composition of Cortical Bone", March 1978), and further in view of **Wolfinbarger, Jr. et al.** (U.S. Patent 6,293,970) and **Ascenzi et al.** ("The torsional properties of single selected osteons", October 1993).

17.1 As per claim 22, **Crolet et al., Carter et al.** and **Wolfinbarger, Jr. et al.** teach the method of claim 21. **Crolet et al.** teaches that the mechanical properties are determined by evaluating hydroxyapatite content (Page 679, CL1, Para 3; Page 679, CL2, Para 1; Page 684 CL2, Para 4).

**Crolet et al.** does not expressly teach that the mechanical properties are determined by evaluating angle-of-twist as a function of torque, strain rate, or time. **Ascenzi et al.** (October 1993) teaches that the mechanical properties are determined by evaluating angle-of-twist as a

function of torque (Abstract; Page 875, CL2, Para 3; Page 880, Fig. 4), as the longitudinal osteons indicate most resistance to torsional loading; and the transverse osteons have low resistance to torsional loading (Abstract, L8-10). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Crolet et al.** with the method of **Ascenzi et al.** (October 1993) that included the mechanical properties being determined by evaluating angle-of-twist as a function of torque. The artisan would have been motivated because the longitudinal osteons would indicate most resistance to torsional loading; and the transverse osteons would have low resistance to torsional loading.

**Crolet et al.** does not expressly teach that the mechanical properties are determined by evaluating an angle-of-twist as a function of strain rate or time. **Ascenzi et al.** (October 1993) teaches that the mechanical properties are determined by evaluating an angle-of-twist as a function of strain rate or time (Page 879, CL1, Para 5 to Page 879, CL2, Para 1), as the osteon failure depends on the strain rate and time (Page 879, CL1, Para 5 to Page 879, CL2, Para 1). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Crolet et al.** with the method of **Ascenzi et al.** (October 1993) that included the mechanical properties being determined by evaluating an angle-of-twist as a function of strain rate or time. The artisan would have been motivated because the osteon failure would depend on the strain rate and time.

17.2 As per claim 23, **Crolet et al., Carter et al., Wolfinbarger, Jr. et al.** and **Ascenzi et al.** (October 1993) teach the method of claim 22.

**Crolet et al.** does not expressly teach that angle-of-twist as a function of torque is determined by quasi-static torsional loading to rupture. **Ascenzi et al.** (October 1993) teaches that angle-of-twist as a function of torque is determined by quasi-static torsional loading to rupture (Page 879, CL1, Para 5 to Page 879, CL2, Para 1; Page 880, CL1, Para 4 to Page 881, CL2, Para 1; Page 880, Fig. 4), as the stress and strain produced during application of the progressive loading allows determination of the unchecked twisting of the specimen indicating osteon failure (Page 879, CL1, Para 5 to Page 879, CL2, Para 1). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Crolet et al.** with the method of **Ascenzi et al.** (October 1993) that included the angle-of-twist as a function of torque being determined by quasi-static torsional loading to rupture. The artisan would have been motivated because the stress and strain produced during application of the progressive loading would allow determination of the unchecked twisting of the specimen indicating osteon failure.

18. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Crolet et al.** ("Compact Bone: Numerical simulation of mechanical characteristics", J. Biomechanics, Vol. 26, No. 6, 1993) in view of **Ascenzi** ("A first estimation of prestress in so-called circularly fibred osteonic lamellae", March 1999), and **Lakes,** ("Materials with structural hierarchy", Nature 361, February 1993), and further in view of **Ascenzi et al.** ("The torsional properties of single selected osteons", October 1993).

18.1 As per claim 16, **Crolet et al.** teaches the model of claim 1. **Crolet et al.** does not expressly teach the model comprising a Finite Element Model (FEM). **Ascenzi et al.** (October 1993) teaches the model comprising a Finite Element Model (FEM) (Page 880, CL1, Para 1), as the mechanical properties of the osteons can be determined by applying finite element analysis (Abstract, L8-10). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the model of **Crolet et al.** with the model of **Ascenzi et al.** (October 1993) that included the model comprising a Finite Element Model (FEM). The artisan would have been motivated because the mechanical properties of the osteons could be determined by applying finite element analysis.

19. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Crolet et al.** ("Compact Bone: Numerical simulation of mechanical characteristics", J. Biomechanics, Vol. 26, No. 6, 1993) in view of **Carter et al.** ("Mechanical properties and composition of Cortical Bone", March 1978), and further in view of **Ascenzi** ("A first estimation of prestress in so-called circularly fibred osteonic lamellae", March 1999), and **Lakes** ("Materials with structural hierarchy", Nature 361, February 1993).

19.1 As per claim 17, **Crolet et al.** teaches the model comprising the viscoelastic properties of longitudinal and alternate osteons (Page 683, CL1, Para 3 and 4).

**Crolet et al.** does not expressly teach a method of predicting deformation and fractures of compact adult bone comprising using a model of compact adult bone. **Carter et al.** teaches a

method of predicting deformation and fractures of compact adult bone comprising using a model of compact adult bone (Page 192, CL1, Para 1; Page 192, CL2, Para 1; Page 198, CL1, Para 2; Page 199, CL2, Para 2 to Page 200, CL1, Para 1), because sustained loading of the cortical bone produces a gradual increase in deformation with time; the rapidity of the deformation or the strain rate depends on the stress-strain behavior of the cortical bone (Page 198, CL1, Para 2); and if the stress magnitude during repeated loading are high enough, fatigue failure may result (Page 200, CL1, Para 1). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the method of **Crolet et al.** with the method of **Carter et al.** that included a method of predicting deformation and fractures of compact adult bone comprising using a model of compact adult bone. The artisan would have been motivated because sustained loading of the cortical bone would produce a gradual increase in deformation with time; the rapidity of the deformation or the strain rate would depend on the stress-strain behavior of the cortical bone; and if the stress magnitude during repeated loading were high enough, fatigue failure might result.

**Crolet et al.** does not expressly teach that each viscoelastic property is correlated with at least one component of bone microstructure and ultrastructure, and components are grouped hierarchically to provide a description of one or more characteristics of the bone. **Ascenzi** (March 1999) teaches that the each viscoelastic property is correlated with at least one component of bone microstructure and ultrastructure, and components are grouped hierarchically to provide a description of one or more characteristics of the bone (Abstract, L1-3, L5-8 and L9-13; Page 935, CL1, Para 1, L3-5), because the use of hierarchical structure involving the microstructure of the osteonic lamellae and the ultra structure of the collagen bundles allows

formulation of hypotheses on lamellar stiffness and other mechanical properties and yields hypotheses on bone ultra- and micro structures (Abstract, L9-13; Page 935, CL1, Para 1, L3-5). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the model of **Crolet et al.** with the model of **Ascenzi** (March 1999) that included each viscoelastic property being correlated with at least one component of bone microstructure and ultrastructure, and components being grouped hierarchically to provide a description of one or more characteristics of the bone. The artisan would have been motivated because the use of hierarchical structure involving the microstructure of the osteonic lamellae and the ultra structure of the collagen bundles would allow formulation of hypotheses on lamellar stiffness and other mechanical properties and would yield hypotheses on bone ultra- and micro structures.

In addition, **Lakes** also teaches that the each viscoelastic property is correlated with at least one component of bone microstructure and ultrastructure, and components are grouped hierarchically to provide a description of one or more characteristics of the bone (Page 5, Fig. 4; Page 5, Para 1, L1-8; Page 1, Para 2, L1-16; Page 2, Para 3, L1-6; Page 5, Par 1, L12-17), because the structural hierarchy can play a major role in determining the bulk material properties; understanding the effects of the hierarchical structure can guide the synthesis of new materials with physical properties tailored for specific applications (Page 1, Para 1); the idea of hierarchical structure can be the basis for synthesis of new microstructures which give rise to enhanced and useful physical properties such as improved strength and toughness (Page 1, Para 2, L16-19). It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to modify the model of **Crolet et al.** with the model of **Lakes** that included each viscoelastic property being correlated with at least one component of bone

microstructure and ultrastructure, and components being grouped hierarchically to provide a description of one or more characteristics of the bone. The artisan would have been motivated because the structural hierarchy could play a major role in determining the bulk material properties; understanding the effects of the hierarchical structure could guide the synthesis of new materials with physical properties tailored for specific applications; the idea of hierarchical structure could be the basis for synthesis of new microstructures which would give rise to enhanced and useful physical properties such as improved strength and toughness.

20. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Crolet et al.** ("Compact Bone: Numerical simulation of mechanical characteristics", J. Biomechanics, Vol. 26, No. 6, 1993) in view of **Carter et al.** ("Mechanical properties and composition of Cortical Bone", March 1978), **Ascenzi** ("A first estimation of prestress in so-called circularly fibred osteonic lamellae", March 1999), and **Lakes** ("Materials with structural hierarchy", Nature 361, February 1993), and further in view of **Ascenzi et al.** ("The torsional properties of single selected osteons", October 1993).

20.1 As per claim 18, **Crolet et al., Carter et al., Ascenzi** (March 1999), and **Lakes** teach the method of claim 17. **Crolet et al.** does not expressly teach that the model simulates fracture propagation by calculating stress distribution as a function of a torque applied to the bone. **Ascenzi et al.** (October 1993) teaches that the model simulates fracture propagation by calculating stress distribution as a function of a torque applied to the bone (Page 879, CL1, Para 5 to Page 879, CL2, Para 1; Page 880, CL1, Para 4 to Page 881, CL2, Para 1; Page 880, Fig. 4),

as the longitudinal osteons indicate most resistance to torsional loading; and the transverse osteons have low resistance to torsional loading (Abstract); fractures produced by torsion differ substantially according to the type of osteon (Page 881, CL1, Para 5 to Page 881, CL2, Para 1). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Crolet et al.** with the method of **Ascenzi et al.** (October 1993) that included the model simulating fracture propagation by calculating stress distribution as a function of a torque applied to the bone. The artisan would have been motivated because the longitudinal osteons would indicate most resistance to torsional loading; and the transverse osteons would have low resistance to torsional loading; and fractures produced by torsion differ substantially according to the type of osteon.

20. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Crolet et al.** ("Compact Bone: Numerical simulation of mechanical characteristics", J. Biomechanics, Vol. 26, No. 6, 1993) in view of **Ascenzi** ("A first estimation of prestress in so-called circularly fibred osteonic lamellae", March 1999), and **Lakes** ("Materials with structural hierarchy", Nature 361, February 1993), and further in view of **Copland III et al.** (U.S. Patent 6,333,313), and **Agrawal et al.** (U.S. Patent 5,947,893).

20.1 As per claim 19, **Crolet et al., Ascenzi** (March 1999), and **Lakes** teach the model of claim 1. **Crolet et al.** does not expressly teach a method of identifying the requirements of bone reconstruction. **Copland III et al.** teaches a method of identifying the requirements of bone reconstruction (CL8, L9-13), as bone reconstruction requires ability to reconstruct defects in

bone tissue resulting from various causes (CL8, L10-13). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Crolet et al.** with the method of **Copland III et al.** that included a method of identifying the requirements of bone reconstruction. The artisan would have been motivated because bone reconstruction requires ability to reconstruct defects in bone tissue resulting from various causes.

**Crolet et al.** does not expressly teach a method of identifying the requirements of prosthesis. **Agrawal et al.** teaches a method of identifying the requirements of prosthesis (Abstract, L1-16), as long term stability of the prosthesis requires bone to form an interlock by growing into the prosthesis at the mating surface (CL1, L43-46). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Crolet et al.** with the method of **Agrawal et al.** that included a method of identifying the requirements of prosthesis. The artisan would have been motivated because long term stability of the prosthesis would require bone to form an interlock by growing into the prosthesis at the mating surface.

21. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Crolet et al.** ("Compact Bone: Numerical simulation of mechanical characteristics", J. Biomechanics, Vol. 26, No. 6, 1993) in view of **Carter et al.** ("Mechanical properties and composition of Cortical Bone", March 1978) and **Wolfinbarger, Jr. et al.** (U.S. Patent 6,293,970), and further in view of **Hamamoto et al.** (U.S. Patent 5,732,469) and **Ascenzi et al.** ("X-Ray diffraction on cyclically loaded osteons", August 1997).

21.1 As per claim 26, **Crolet et al., Carter et al.** and **Wolfinbarger, Jr. et al.** teach the method of claim 21. **Crolet et al.** does not expressly teach that the collagen-bundle direction related to osteon axis is determined by circularly polarizing light microscopy, confocal microscopy or X-ray diffraction. **Hamamoto et al.** teaches that the collagen-bundle direction related to osteon axis is determined by circularly polarizing light microscopy or confocal microscopy (CL9, L44-46; CL19, L34-37), as the degree of penetration of the osteoblast can be examined by light microscopy (CL19, L34-37). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Crolet et al.** with the method of **Hamamoto et al.** that included the collagen-bundle direction related to osteon axis being determined by circularly polarizing light microscopy or confocal microscopy. The artisan would have been motivated because the degree of penetration of the osteoblast could be examined by light microscopy.

**Crolet et al.** does not expressly teach that the collagen-bundle direction related to osteon axis is determined by X-ray diffraction. **Ascenzi et al.** (August 1997) teaches that the collagen-bundle direction related to osteon axis is determined by X-ray diffraction (Abstract), as the structural distortions induced by the cyclic loading can be investigated by X-ray diffraction (Abstract, L12-14). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Crolet et al.** with the method of **Ascenzi et al.** (August 1997) that included the collagen-bundle direction related to osteon axis being determined by X-ray diffraction. The artisan would have been motivated because the structural distortions induced by the cyclic loading can be investigated by X-ray diffraction.

## ***Response to Arguments***

22. Applicant's arguments filed on November 15, 2004 have been fully considered. The arguments with respect to 102 (e) and 103 (a) rejections are not persuasive.

22.1 As per the applicants' argument that "Crolet does not assemble groups of osteons into a model of macroscopic properties of an entire bone, e.g., a femur; Crolet disregards the dynamic hierarchy of bone structure because it makes unrealistic estimates of structure (e.g., "averaging" osteon structure) and viscoelastic properties (e.g., assuming linear elasticity); the lack of recognition and use of the hierarchical structural and viscoelastic properties limit the Crolet model; ... Crolet does not account for the hierarchical structural classification of bone including bone microstructure and ultrastructure, and further does not correlate the viscoelastic properties with structure; Crolet also does not include "the viscoelastic properties of at least one type of osteon" but instead estimates an entire osteon based purely on theory; further, static loading, not dynamic loading, is used to evaluate bone characteristics; this simplification does not meaningfully account for the viscoelastic properties of bone, particularly for trauma and fracture situations; ... Crolet does not disclose collagen content, hydroxyapatite content, collagen bundle orientation, and content of porosity fluids as the examiner contends, but instead assumes that collagen fiber and the hydroxyapatite are homogeneous, isotropic and linearly elastic and that collagen is perfectly embedded in hydroxyapatite without lacunae and with a rigid interface; Crolet also does not account for the specific location of biological fluids in bone; such an over-simplification does not account for the dynamic microstructure and ultrastructure of bone;

Crolet then makes groups of osteons which are not homogeneous, however, groups of these osteons cover only a small region of an actual bone; at best, Crolet provides a "partial" over-simplified model of bone", the examiner has used new references, **Ascenzi** (March 1999), and **Lakes** (February 1993).

**Ascenzi** (March 1999) teaches that the each viscoelastic property is correlated with at least one component of bone microstructure and ultrastructure, and components are grouped hierarchically to provide a description of one or more characteristics of the bone (Abstract, L1-3, L5-8 and L9-13; Page 935, CL1, Para 1, L3-5), because the use of hierarchical structure involving the microstructure of the osteonic lamellae and the ultra structure of the collagen bundles allows formulation of hypotheses on lamellar stiffness and other mechanical properties and yields hypotheses on bone ultra- and micro structures (Abstract, L9-13; Page 935, CL1, Para 1, L3-5).

**Lakes** also teaches that the each viscoelastic property is correlated with at least one component of bone microstructure and ultrastructure, and components are grouped hierarchically to provide a description of one or more characteristics of the bone (Page 5, Fig. 4; Page 5, Para 1, L1-8; Page 1, Para 2, L1-16; Page 2, Para 3, L1-6; Page 5, Par 1, L12-17), because the structural hierarchy can play a major role in determining the bulk material properties; understanding the effects of the hierarchical structure can guide the synthesis of new materials with physical properties tailored for specific applications (Page 1, Para 1); the idea of hierarchical structure can be the basis for synthesis of new microstructures which give rise to enhanced and useful physical properties such as improved strength and toughness (Page 1, Para 2, L16-19). **Lakes** also teaches anisotropy of the lamina and predicting the anisotropic elasticity of the bone.

22.2 As per the applicants' argument that "Carter does not cure the deficiencies in Crolet. ...the disclosure of Carter is based on an oversimplified collagen apatite distribution model; while Wolfinbarger mentions that bone tissue is comprised of osteoid, e.g., mucopolysaccharides, and minerals, it teaches a plasticized dehydrated or freeze-dried bone product that approximates properties in normal bone...there is no suggestion or motivation to combine the reference teachings to arrive at the model of claims 3, 4, 11, and 21; both Crolet and Wolfinbarger teach broad assumptions of the structure of bone, and Carter examines one portion of the heterogeneous structure; the combination of references does not suggest a model comprising the claimed complex characteristics, e.g., viscoelastic properties" of an osteon, such as "mechanical properties, collagen content, mucopolysaccharide content, hydroxyapatite content, collagen bundle orientation relative to the osteon axis, osteocyte content, osteoblast content, and content of porsity fluids." The combination further does not provide a model that accounts for bone microstructure, bone ultrastructure in connection with the viscoelastic properties", the examiner has used new references, **Ascenzi** (March 1999), and **Lakes** (February 1993). The combination of **Ascenzi** (March 1999), and **Lakes** (February 1993) provide a model that accounts for bone microstructure, bone ultrastructure in connection with the viscoelastic properties as explained in Paragraph 22.1 above.

22.3 As per the applicants' argument that "The addition of Ascenzi I does not overcome the shortcomings of Crolet, Carter, and Wolfinbarger to arrive at claims 5, 6, 22, and 23. There is no suggestion or motivation in the references to combine the teachings to arrive at the novel claimed

model;... the FEM in Ascenzi I would not render the claimed model of viscoelastic properties of an osteon including FEM obvious; ... An assumption that the combination obviates claim 16 is based upon improper hindsight reasoning, reached only by examination of the instant application", the examiner respectfully disagrees.

**Ascenzi et al.** (October 1993) teaches that osteon mechanical properties comprises an angle-of-twist as a function of torque (Abstract; Page 875, CL2, Para 3; Page 880, Fig. 4), as the longitudinal osteons indicate most resistance to torsional loading; and the transverse osteons have low resistance to torsional loading (Abstract, L8-10). **Ascenzi et al.** (October 1993) teaches that osteon mechanical properties comprises an angle-of-twist as a function of strain rate or time (Page 879, CL1, Para 5 to Page 879, CL2, Para 1), as the osteon failure depends on the strain rate and time (Page 879, CL1, Para 5 to Page 879, CL2, Para 1). **Ascenzi et al.** (October 1993) teaches that the angle-of-twist as a function of torque is derived from tests conducted under monotonic or dynamic loading (Page 879, CL1, Para 5 to Page 879, CL2, Para 1; Page 880, CL1, Para 4 to Page 881, CL2, Para 1; Page 880, Fig. 4), as the stress and strain produced during application of the progressive loading allows determination of the unchecked twisting of the specimen indicating osteon failure (Page 879, CL1, Para 5 to Page 879, CL2, Para 1). **Ascenzi et al.** (October 1993) teaches the model comprising a Finite Element Model (FEM) (Page 880, CL1, Para 1), as the mechanical properties of the osteons can be determined by applying finite element analysis (Abstract, L8-10).

22.4 As per the applicants' argument that "the combination of Crolet, Carter and Ascenzi I does not render the claimed model of bone obvious because it would be based upon the osteon

homogenization theory and incomplete bone characterization of Crolet; accordingly, a method of predicting deformation using such a model would not have been obvious based upon the combination of prior art teachings that suggest nothing more than a mathematical model and isolated experimentation upon portions of bone", the examiner has used new references, **Ascenzi** (March 1999), and **Lakes** (February 1993) in addition to Crolet, Carter and Ascenzi I. The combination of **Ascenzi** (March 1999), and **Lakes** (February 1993) provide a model that accounts for bone microstructure, bone ultrastructure in connection with the viscoelastic properties as explained in Paragraph 22.1 above. **Lakes** also teaches anisotropy of the lamina and predicting the anisotropic elasticity of the bone.

22.5 As per the applicants' argument that "Crolet, Copeland III and Agrawal in combination do not render claim 19 obvious because none of the references teach or suggest the inventive model, and further do not suggest identification of the requirements of bone reconstruction and prosthesis using such a model", the examiner respectfully disagrees.

**Copland III et al.** teaches a method of identifying the requirements of bone reconstruction (CL8, L9-13), as bone reconstruction requires ability to reconstruct defects in bone tissue resulting from various causes (CL8, L10-13). **Agrawal et al.** teaches a method of identifying the requirements of prosthesis (Abstract, L1-16), as long term stability of the prosthesis requires bone to form an interlock by growing into the prosthesis at the mating surface (CL1, L43-46).

22.5 As per the applicants' argument that "the cited combination does not suggest the claimed method using a realistic bone model, wherein one portion of the model, collagen-bundle direction, is determined by microscopy techniques or X-ray diffraction; instead, the combination of references would, at best, suggest a mathematical model assuming that bone structure is homogenous, in combination with experimental studies on components of bone and bone prosthesis products", the examiner directs the applicants attention to the fact that claim 26 and claim 20 on which it depends do not require non-homogeneous bone structure.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Kandasamy Thangavelu whose telephone number is 571-272-3717. The examiner can normally be reached on Monday through Friday from 8:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kevin Teska, can be reached on 571-272-3716. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-305-9600.

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K. Thangavelu
Art Unit 2123
February 14, 2005

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